

Longevity Supplements: Marketing & Substantiation Guidelines to Stand the Test of Time

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Longevity Overview

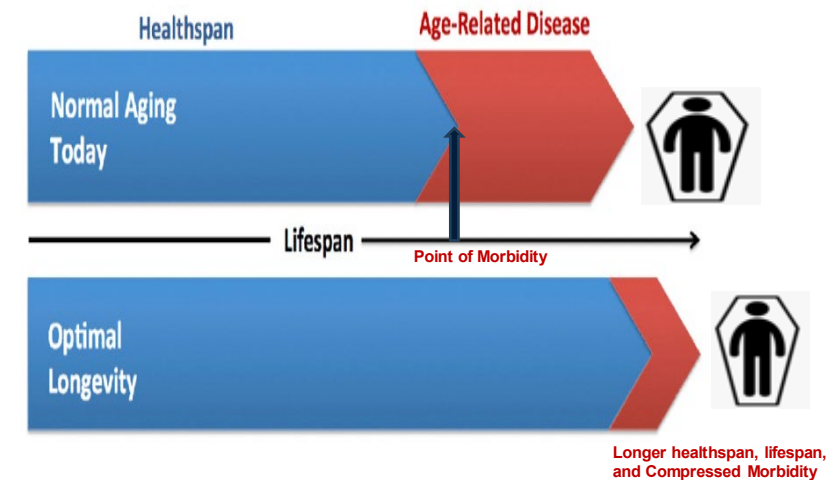
Healthy Aging Strategies According to Mark Twain



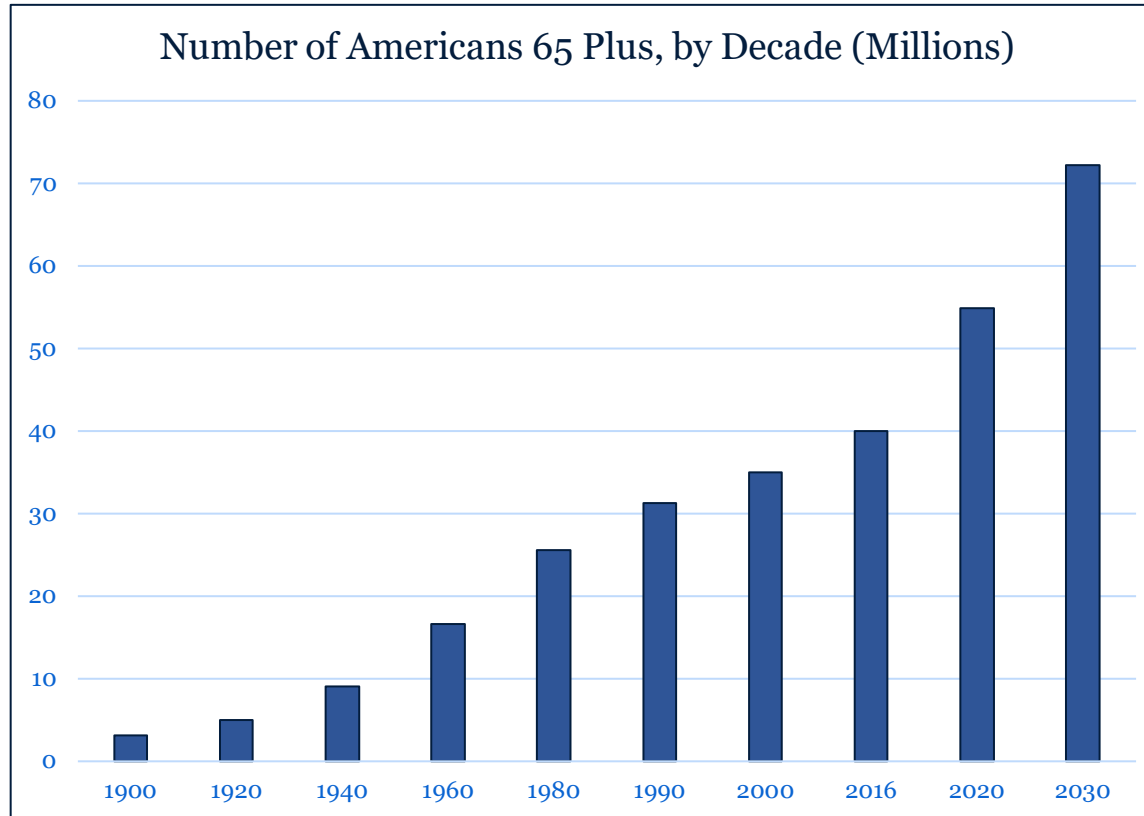
- “Life would be infinitely happier if we could only be born at the age of eighty and gradually approach eighteen.”
Autobiography with Letters, William L. Phelps
- Whatever a man's age, he can reduce it several years by putting a bright-colored flower in his button-hole.
The American Claimant

Some (Modern) Definitions That Are Often Confused/Interchanged

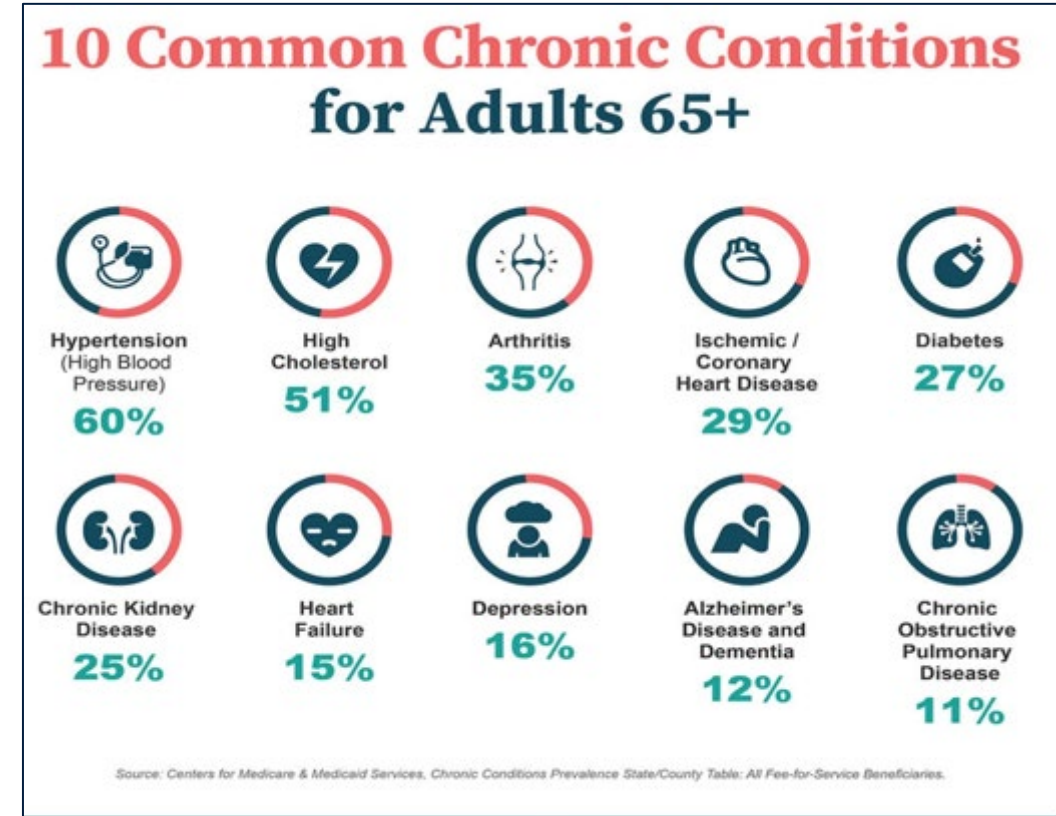
- **Longevity:** Living a life longer than the average, at age of death.
- **Lifespan:** The average maximum time one or more people survive between birth and death.
- **Healthspan:** The healthy years of lifespan.
- **Morbidity:** The years of declining health, increasing disease.
- **Age:** What's on your passport.
- **Biological Age:** How old your _____ thinks you are.



Aging Is Not a Disease... but It Ushers in a Host of Them



USA Census Data, 2020.



Infographic: National Council on Aging, 2023.

What is a Claim?

Explicit or implicit statement that a product has a certain benefit

- Explicit: “Sugar Free,” “High in fiber,” “Low Calories,” “Non-GMO,” “Immune Support”
- Implicit: Use of pictures of fruit or vegetables on a product label (*i.e.*, a product contains whole fruit or vegetables); Imagery of a grandparent doing physical activity with ease (*i.e.*, no joint pain)

All claims are:

- Held to specific standards of substantiation
- Evaluated on a “net impression”
 - **All** elements included (text, names, pictures, testimonials, etc.)

Again: Claims drive product classification and in turn what regulations apply

Structure/Function Claims

- Characterizes how a dietary ingredient or nutrient affects normal structure or function in humans
 - “Supports,” “Promotes,” “Improves,” etc.
 - Fine line between these claims and other claims; requires careful phrasing and qualification
 - **Highly context-dependent; one claim may be permissible in one setting and impermissible in another**
- Requires a notification to FDA within 30 days of first marketing a claim
- All structure/function claims must link to the DSHEA disclaimer:
 - “This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.”

Structure/Function Claims

Construction of a Permissible Structure/Function Claim

- [FDA Final Rule on Structure/Function Claims \(Jan. 6, 2000\)](#)
 - Defines the types of statements allowed concerning a dietary supplement's effects on the structure or function of the body
 - Addresses industry comments to the rule and agency responses

Key Takeaway: A structure/function claim may not reference, either explicitly or implicitly, a disease state

- Example: Digestive Claims
 - “Alleviates constipation” → Impermissible claim; suggests bowel obstruction or irritable bowel syndrome
 - “For relief of occasional constipation” → Permissible claim; speaks to constipation related to non-disease conditions (*e.g.*, travel, diet change)

FDA vs. FTC Advertising

- FDA is primarily responsible for claims on *labeling*, whereas FTC has responsibility for claims in all forms of advertising.
- FTC does not distinguish between types of health-related products or claims.
- While FDA considers dietary supplements, food, etc. in separate categories, FTC does not.
- FTC does not distinguish between a structure/function claim or another kind of claim.
- However, health claims that meet FDA's scientific standard are presumed to be substantiated.



Health and Longevity Claims

Health and Longevity Claims

Examples

- “Your chronological age can be different from your cellular age”
- “Defend against cellular aging from within”
- “Specially designed formula provides antioxidant support at the cellular level, where aging begins”
- “Encourages youthful cognitive function”
- “Reverse the signs of aging”



The Standard for Substantiating Health and Longevity Claims



Competent and reliable scientific evidence applies, as well as all reasonable inferences.



Animal studies are insufficient.



Increasing the life of a fruit fly or even a rat is not substantiation.



In vitro studies, while useful, still cannot alone substantiate health and longevity claims.



Short-term, double-blind, placebo-control trials are not going to substantiate longevity claims but may support health claims.

Crafting Health and Longevity Claims



- Chronological age is simply your physical age — it cannot change.
- It is what it is ... you may be able to make yourself look younger or have the mental capacity of someone younger, but you are still a certain age.
- Actuarial tables are not that far off if you live a typical life.
- The claim that you look 10 years younger is a comparison that on average you look the same age as someone 10 years younger.
- This can be verified through objective assessment but does not mean you will live longer.
- When crafting health and longevity claims, you must avoid this implication.

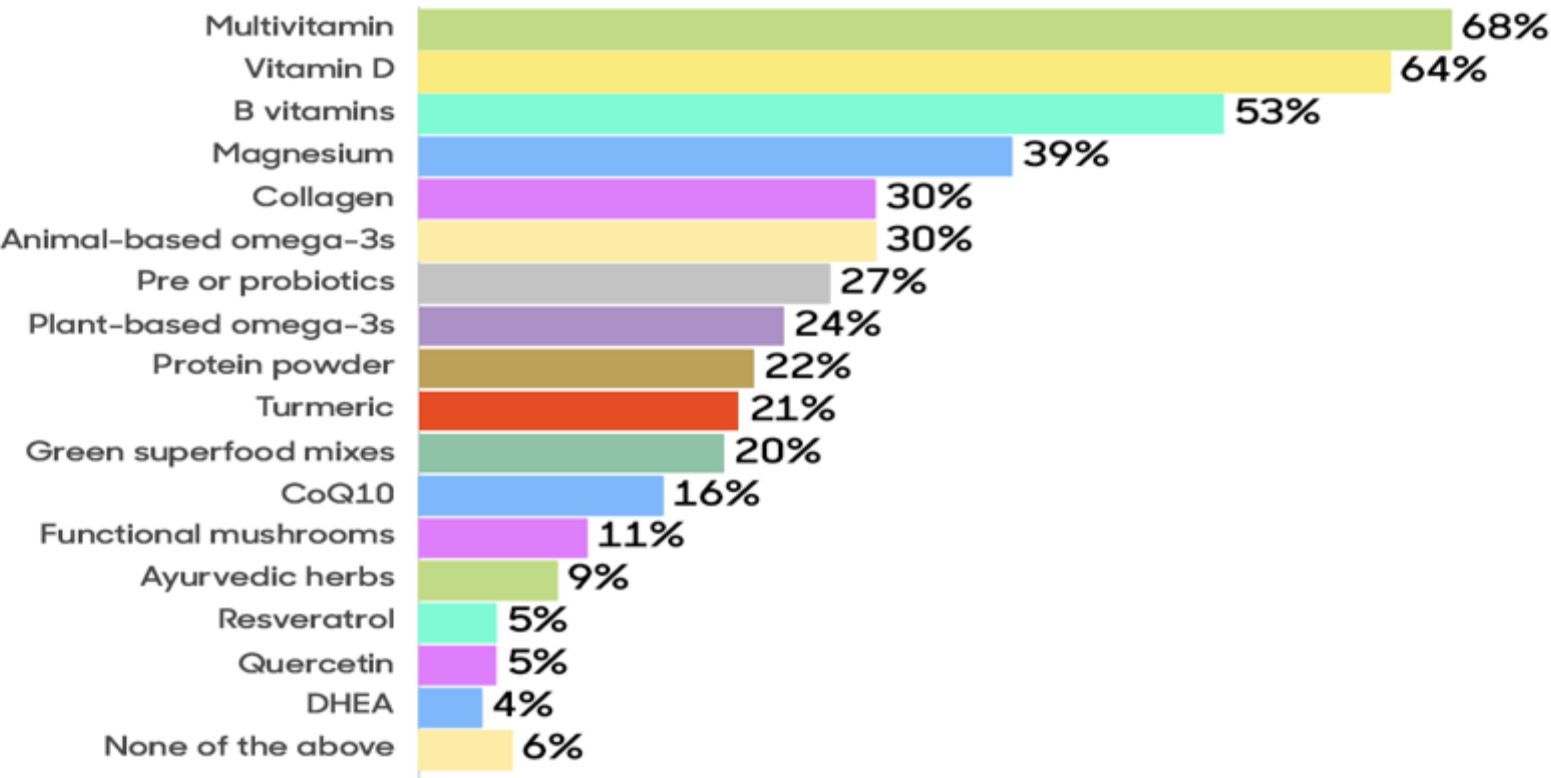
Crafting Health and Longevity Claims (cont.)

- Biological age is complex and includes not only a numerical age but also physiological changes such as methylation of DNA, inflammation, genetics, and lifestyle (nutrition, exercise, alcohol, drug use, smoking, etc.).
- However, from a cellular point of view, you could have all the biomarkers of a 30-year-old and die due to an unforeseen heart condition, such as undiagnosed atrial fibrillation, that caused you to have a stroke. Or just simply to genetics.
- To suggest you can make an unqualified longevity claim is simply not substantiated even if a fruit fly lived longer, or a nutrient appears to activate the “longevity gene.”
- Simply stated, biological age is more an indicator of health span than longevity.

See Maltoni R. et al., Chronological age or biological age: What drives the choice of adjuvant treatment in elderly breast cancer patients? Transl. Oncol. 2022 Jan;15(1):101300. doi: 10.1016/j.tranon.2021.101300. Epub 2021 Dec 1. PMID: 34864401; PMCID: PMC8640726

Marketing Longevity

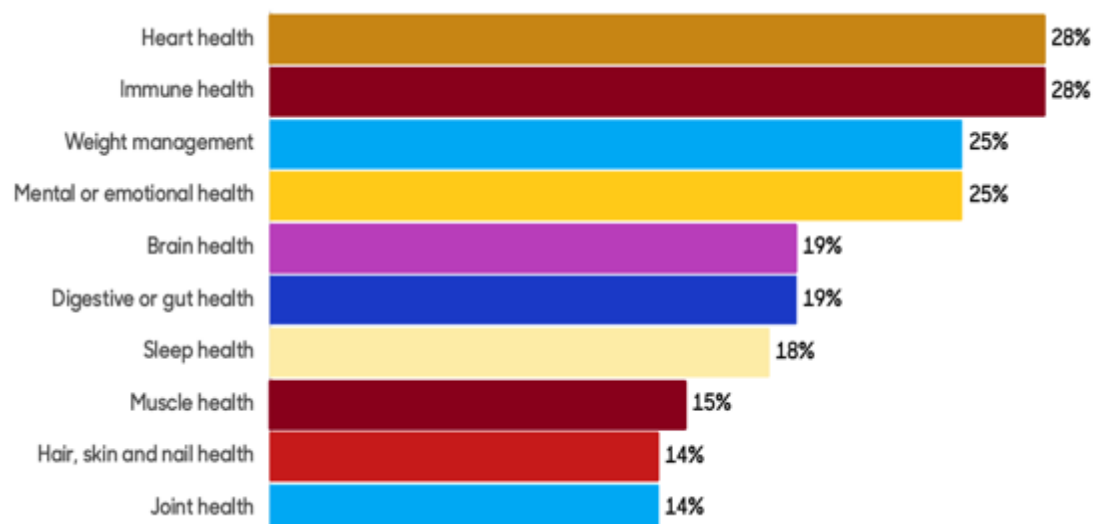
Ingredients Supplement Consumers Believe Will Improve Their Healthspan or Lead to Healthy Aging



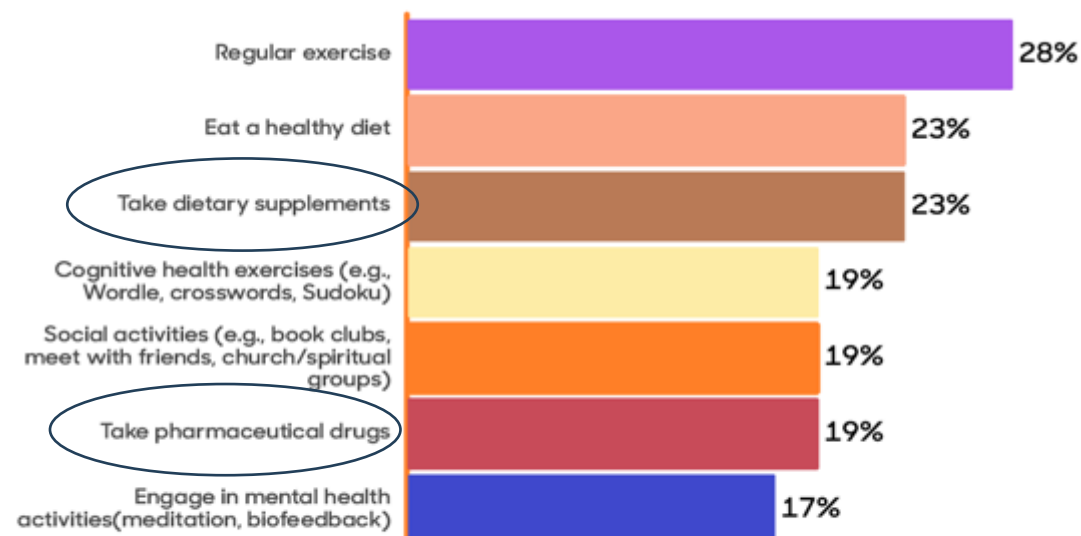
Source: NBJ Longevity Report 2024. Nutrition Business Journal Online Survey: 1010 dietary supplement users, aged 19-75. (Survey completed July 2024).

Consumers Know It, and Are Trying to Combat It

Top 10 Age-related health concerns

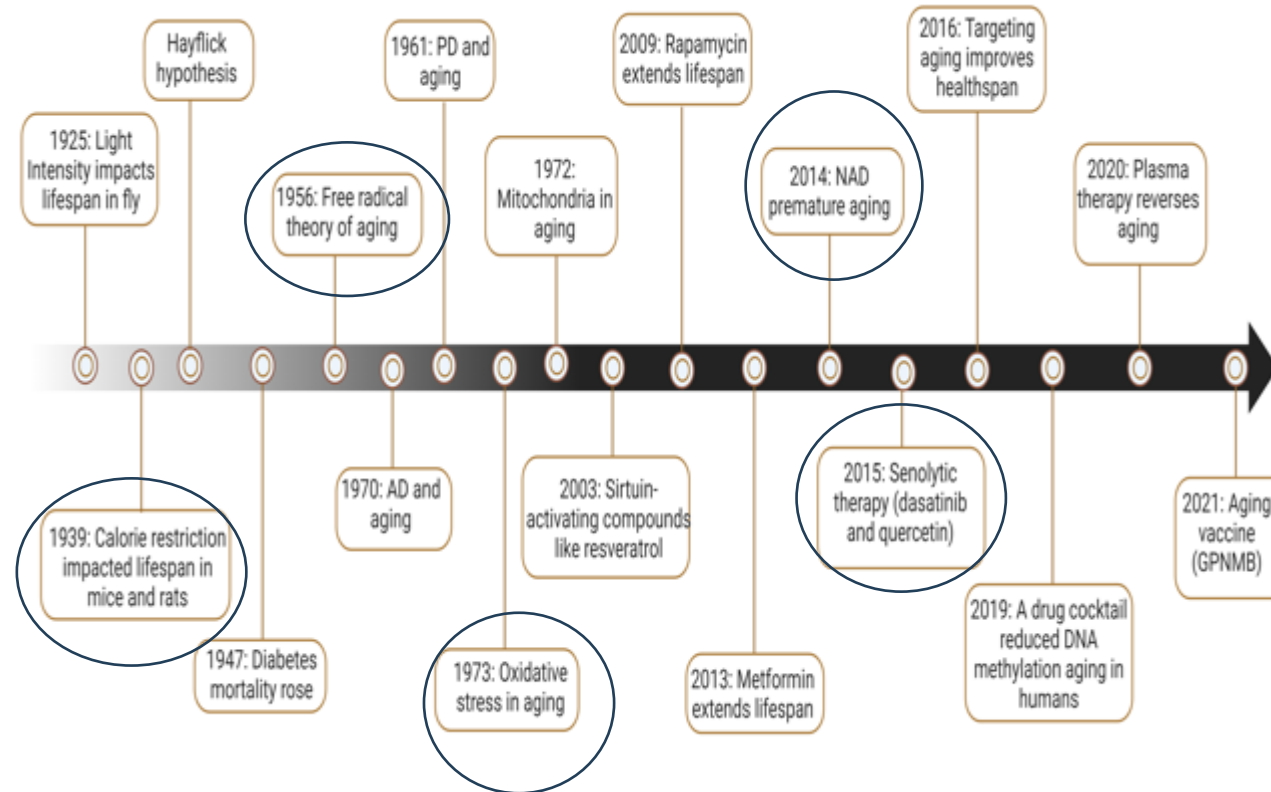


Strategies to extend lifespan

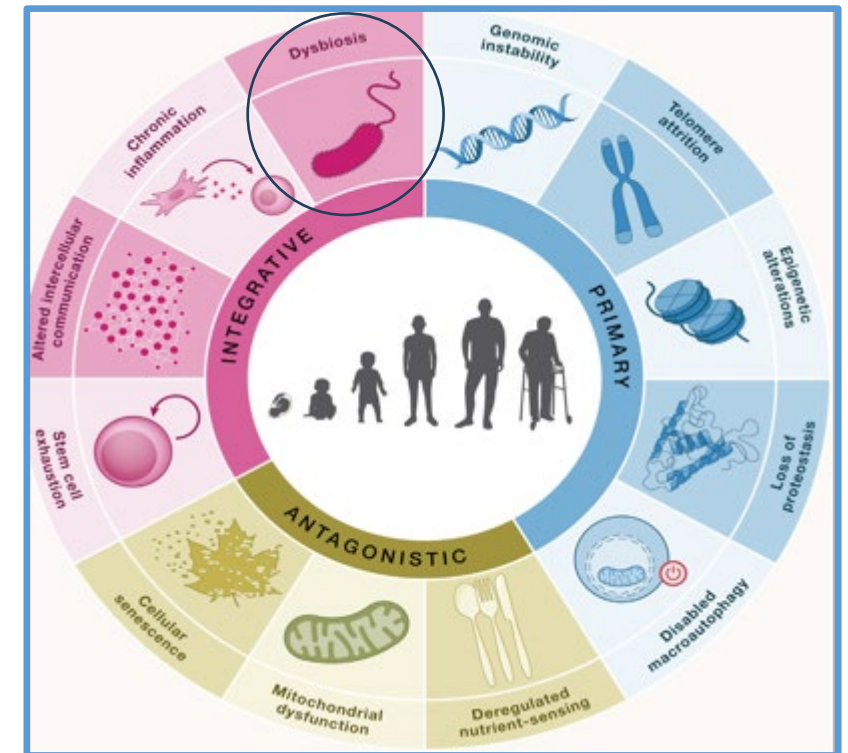


Source: NBJ Longevity Report 2024. Nutrition Business Journal Online Survey: 1010 dietary supplement users, aged 19-75. (Survey completed July 2024)

Milestones in Research-Based Therapeutics

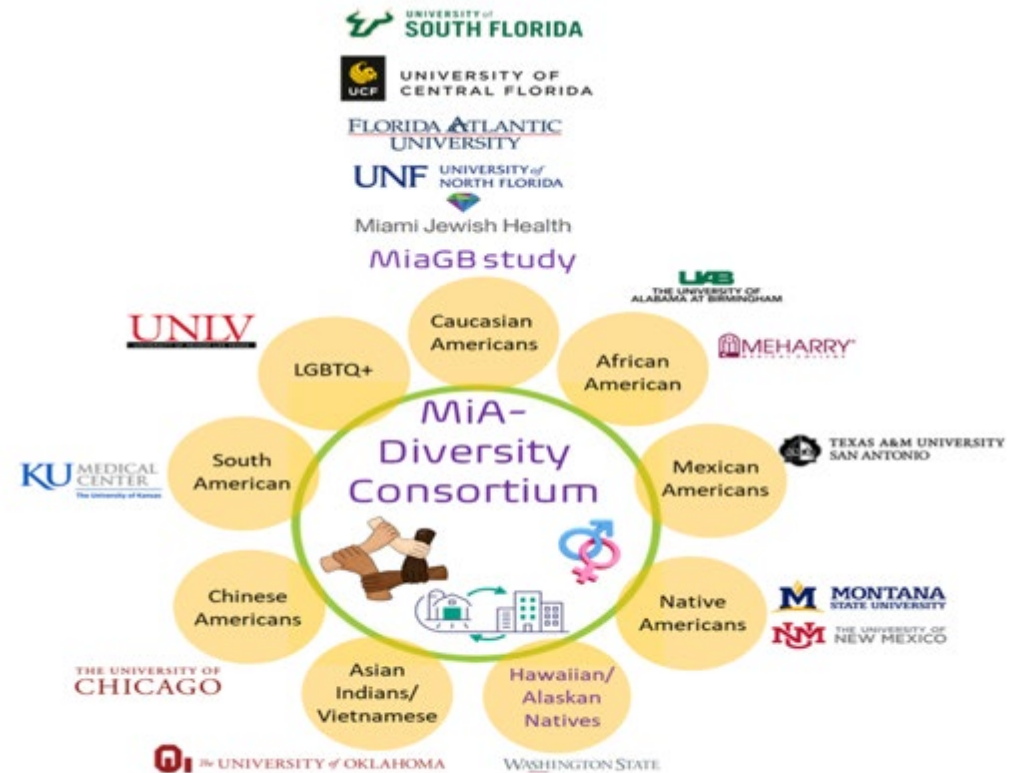
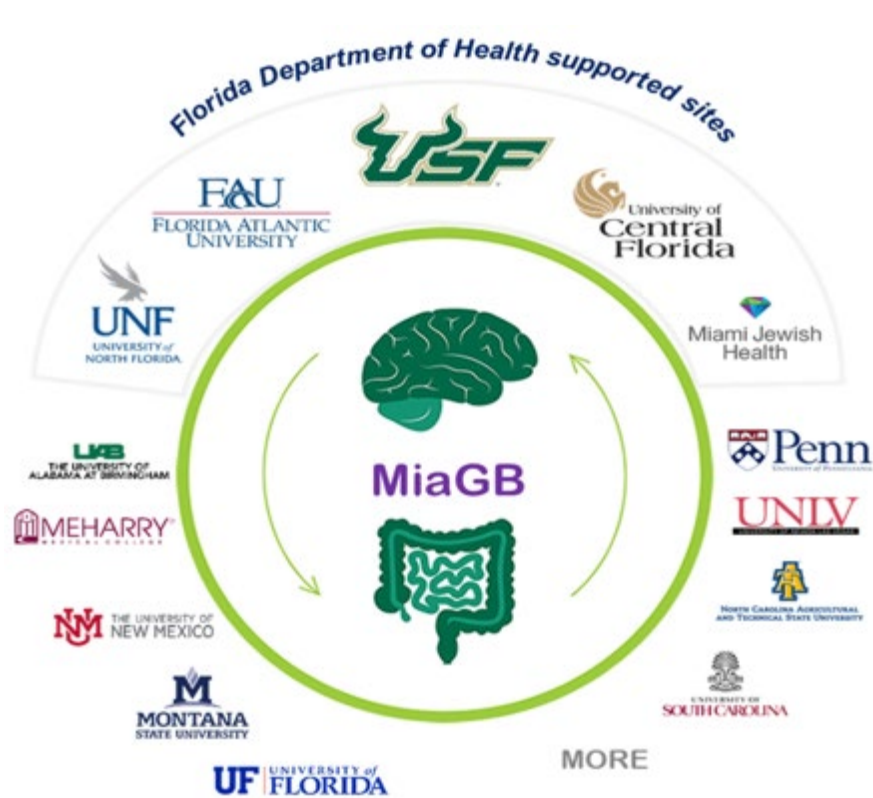


Source: MusB Research, Tampa Longevity CRO.



Hallmarks of Aging, an Expanding Universe,
Cell 186, January 19, 2023.

2023 Largest Consortium in the World on Establishing Ultimate Biological Aging Clock



Typical Timelines of Private Longevity Research - CRO

Preclinical Screening (2-6 months)*



Animal Studies (3-9 months)*



Human Trials (9-15 months)*



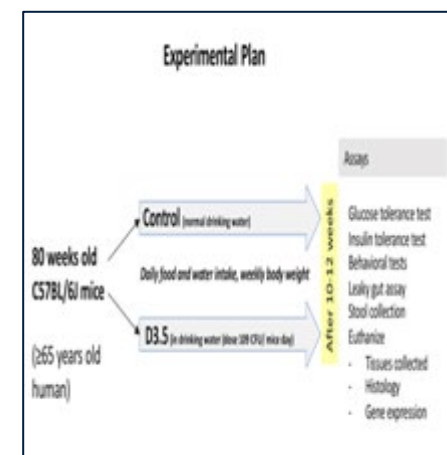
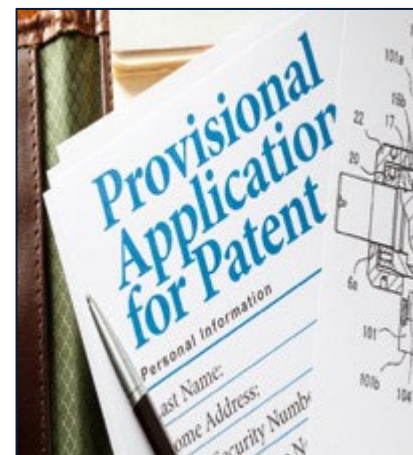
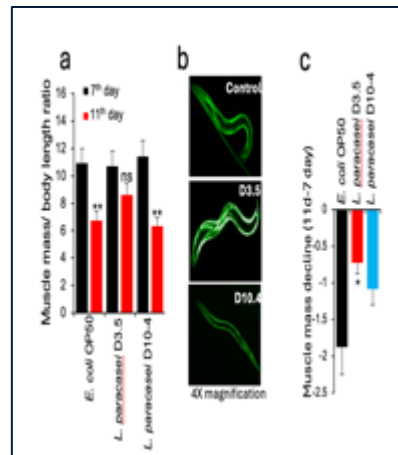
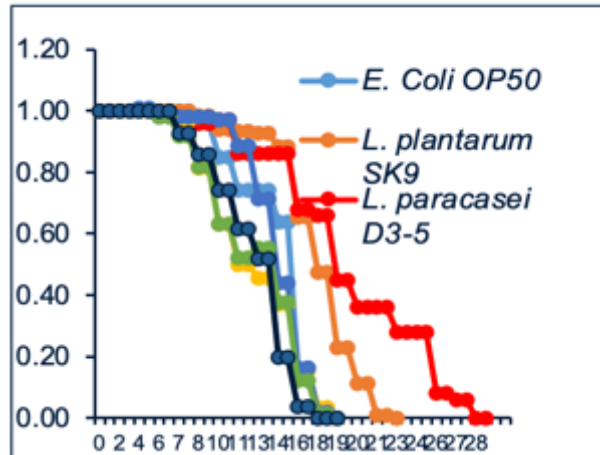
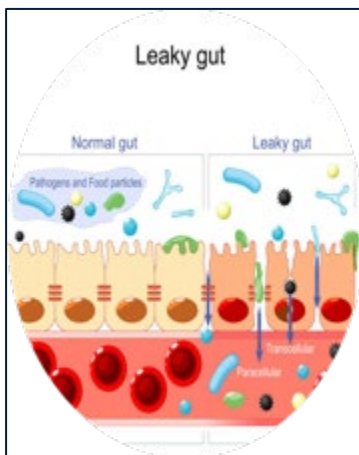
<https://musbresearch.com/services/>

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Case Study: From Plate to the People

Wake Forest College of Medicine: Research to Supplement



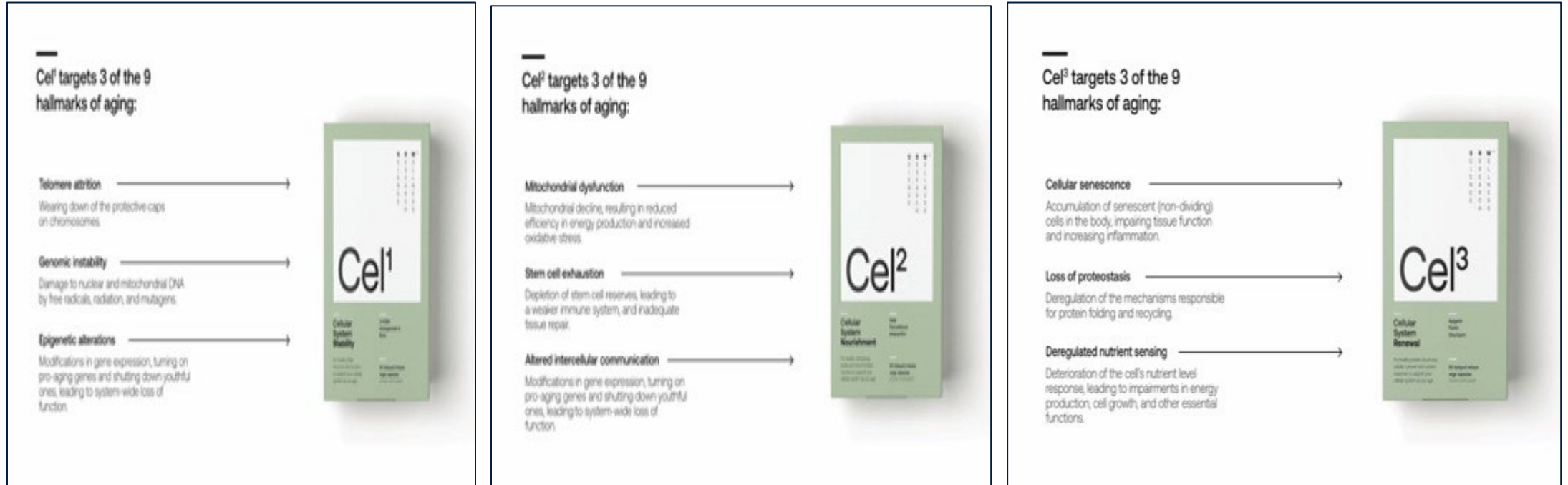
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Longevity Products and Services

Please note, inclusion of these examples does not endorse claims being made by the companies; however, they are interesting case studies in their own right

Hallmark-Based Brand, SRW (New Zealand)



Centarix (Israel) – Clinic for Hallmarks of Aging



TEAM

Over 60 dedicated personnel specializing in various STEM fields such as the biology of aging, molecular and cellular biology, lab automation, bioinformatics, algorithms, and software development



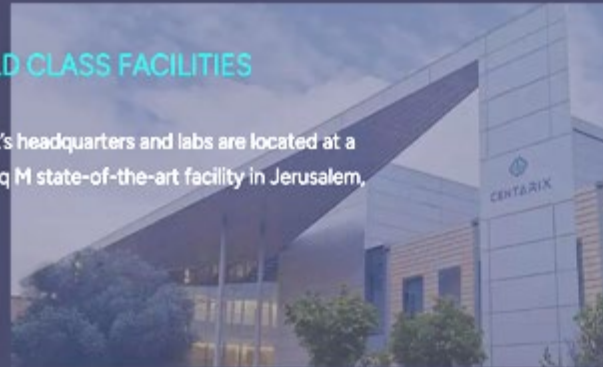
CLINICAL STUDIES

Centarix has conducted a groundbreaking three-year, longitudinal clinical study involving hundreds of subjects, creating a first-of-its-kind aging diagnostic profile.



WORLD CLASS FACILITIES

Centarix's headquarters and labs are located at a 4,000 Sq M state-of-the-art facility in Jerusalem, Israel.



LONGEVITY CLINIC

Centarix owns and runs Centa, the world's most advanced longevity diagnostics and treatment clinic.



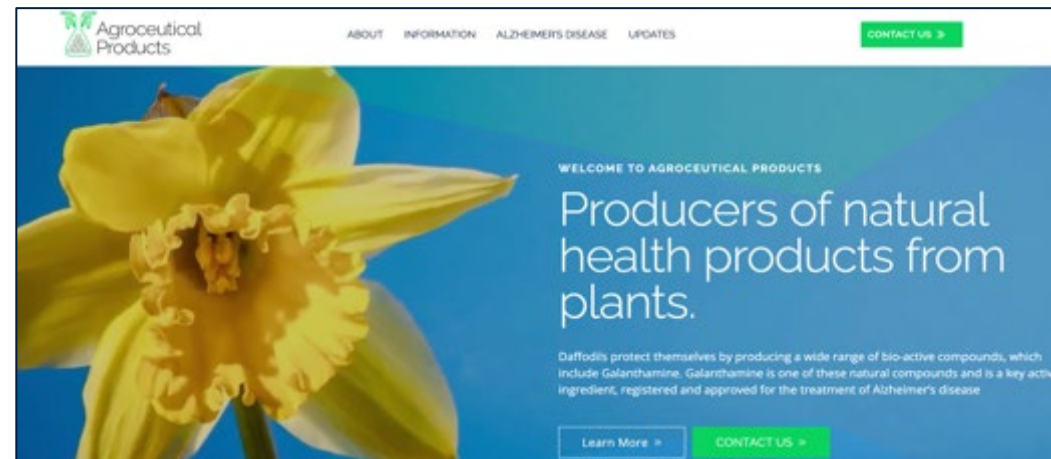
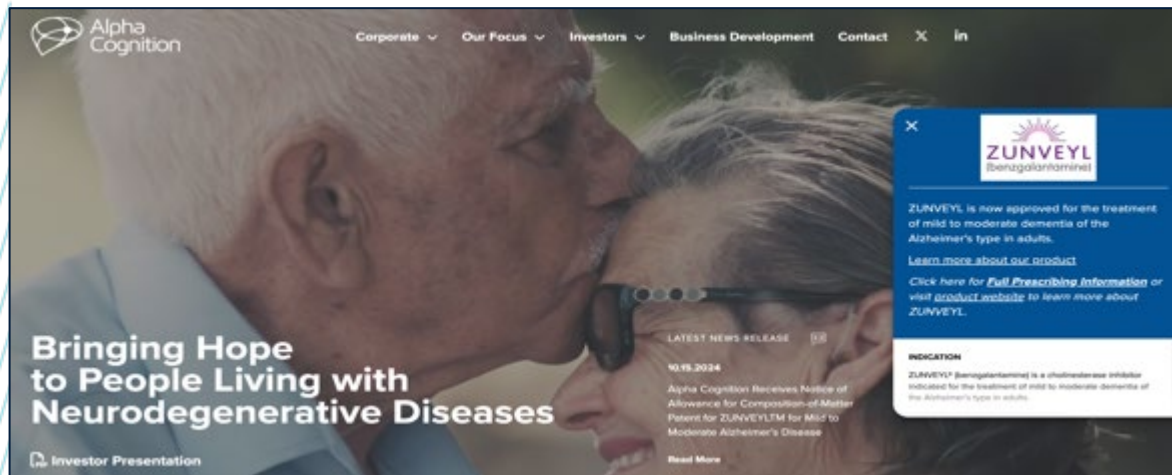
Athletic Greens (AG1) – UK Campaign 8/2024



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Neurodyn Technologies/ Alpha Cognition (Canada): Gut-Brain Supplements / Rx AD



Longevity Solutions for a Healthier, Longer Life



Top Longevity Supplements
and Anti-Aging Solutions



Healthy Aging: Products and
Tips for Aging Well



Gut Health: Supplements and
Solutions for a Healthy Gut



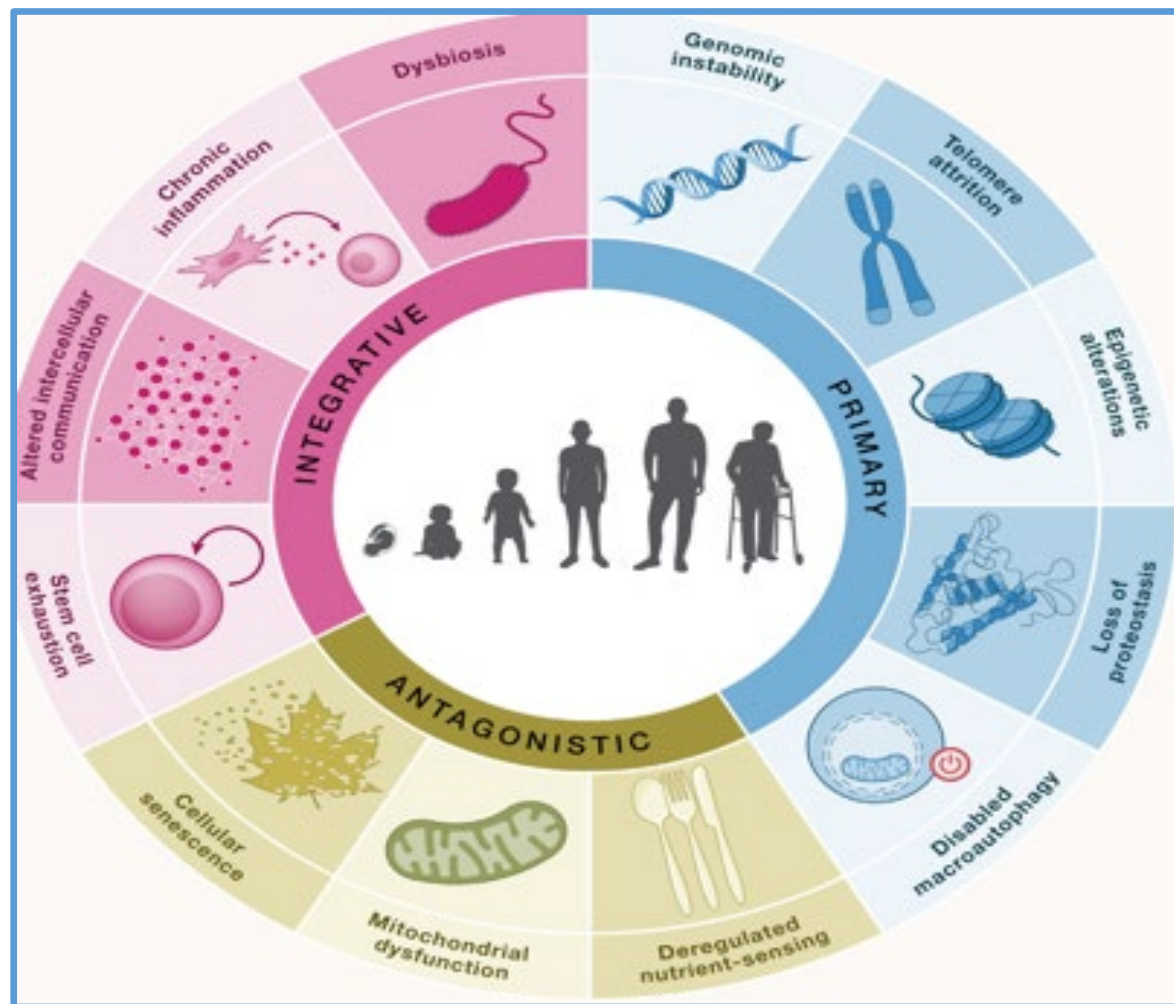
Brain Health: Enhancing
Cognitive Function and Gut-
Brain Connection



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Wheel of (your company's) Fortune?



Questions? Contact me



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Join Todd and the Venable Team at Supply Side West 2024 in Las Vegas on October 30-31.

Venable is excited to once again serve as the official legal and regulatory sponsor of SupplySide West. Attorneys from our FDA, Advertising and Marketing, and Intellectual Property Practice Groups will be available for private consultations in our dedicated meeting space.

Learn more and request a consultation: <https://bit.ly/4evkRp4>

Appendix

What Does Substantiation Mean?

FTC's Substantiation Standard

- Competent and Reliable Scientific Evidence (**CARSE**)
 - Historically, the CARSE standard permits full and careful consideration of a wide range of relevant scientific evidence.
 - Double-blind, randomized, placebo-controlled studies have not been explicitly required for dietary supplement advertising.
- FTC **now** explains that generally, “substantiation of health-related benefits will need to be in the form of randomized, controlled human clinical testing to meet the competent and reliable scientific standard.”
- The **quality of studies relied upon** is also now a focus of the agency:
 - Will evaluate based on control group, randomization, double blinding, statistically significant results, and clinically meaningful results.
 - To determine if clinically meaningful, will consider clarity of the protocol, submission of protocol to an IRB, registration of the clinical trial in a public database, duration of the study, dropout rates, noncompliance, dose-response relationship, and more.

Substantiating Your Claims

The general substantiation rules still apply, such that an advertiser must have a “reasonable basis” for any verifiable claim that is not puffery (whether express or implied) — i.e., the advertiser must have objective evidence that supports the claim.

FTC considers the following in determining what level of support is reasonable:

- Type of claim
- The product
- The consequences of a false claim
- The benefits of a truthful claim
- Ease and cost of developing substantiation for the claim
- The amount of substantiation experts in the field believe is reasonable

However, FTC will likely place greater emphasis in its evaluation of a company’s substantiation on the **quality, type, and amount** of substantiation, as well as the extent to which that substantiation **relates to the claims** being made.

What Are the Key Factors in Determining the Type and Amount of Substantiation Required?

- RCTs are generally the type of substantiation that experts would require for health benefit claims.
 - No requirement for the number — replication adds to the weight
 - Quality is more important than quantity
- Epidemiological/observation studies can substantiate a claim where RCTs aren't otherwise feasible or experts in the field consider it acceptable, but otherwise don't prove a causal link.
- Animal and *in vitro* studies are not sufficient to substantiate health-related claims.
- Anecdotal evidence of consumer experience and surveys are never sufficient (same with HCP's observation of the effect of a health product on patients).
- Public health recommendations are not sufficient to establish a causal link or to support a claim.

What Are the Key Quality Factors?

Study quality will generally be evaluated by considering:

- Control group
- Randomization
- Double blinding
- Statistically significant results
- Clinically meaningful results

To determine if **clinically meaningful**, consider:

- Clarity of the protocol
- Submission of protocol to an IRB
- Registration of the clinical trial in a public database
- Inclusion/exclusion criteria
- Duration of the study
- Dropout rates
- Noncompliance
- Dose-response relationship
- Quality of written report

Other Quality Factors

- Validation
- Temporal nature of effect
- Number of subjects
- Health of subjects (all healthy or have disease/condition)
- Statistical significance is more critically evaluated — FTC is concerned about post hoc analysis and “p-hacking”
- Application of the study results to the claimed benefit
- Absence of contrary evidence, if substantiation is weak, will not help

Totality of the Evidence and Relevance to the Claim

Totality of the Evidence

- Cannot discount research that does not support a claimed effect
- Consistency with surrounding body of evidence
- Explanation for inconsistencies
 - E.g., differences in dosage for route of administration, populations tested, or methodology

Relevance to the Claim

- Similarity of dosage and formulation studied to advertised product
- Similar route of administration
- Study outcomes vs. benefits advertised
- Representation of research results
- Emerging science as basis for a claim: qualifications are important

Substantiation Dossier

- Retaining substantiation often involves maintaining some type of file or dossier dedicated to claims substantiation.
- A substantiation dossier will look different depending on what information you need to keep on file to support your advertising claims, but examples could include:
 - A digital folder where the organization can organize and store any communications, certifications, etc. that support the organization's advertising claims;
 - A substantiation sheet listing information relevant to substantiation, potentially including relevant links if it is stored online;
 - A substantiation chart summarizing relevant sources (particularly common for companies that need to support advertising claims with a variety of clinical studies); or
 - Any other format that makes sense contextually and is easy to reference.
- **The form in which substantiation is stored is less important than the fact that it exists and can be found when it is needed.**

Substantiation Dossier (cont.)

- The documentation that is necessary to substantiate a claim varies depending upon the claim that is being made.
- FTC does not have specific requirements for which documents are required to support every possible type of claim, but at a minimum, when a claim is express (e.g., “tests prove,” “doctors recommend,” and “studies show”), Essential Formulas should have **at least the advertised level of substantiation.**
- Keep in mind that some claims, such as claims involving statistical estimates, are more difficult to substantiate than others.

Disclosures

When is a disclosure required?

- If an ad makes express or implied claims that are likely to be misleading without certain qualifying information, the information must be disclosed.
- A disclosure cannot cure a false claim; it can only qualify or limit a claim to avoid a misleading impression.
- Disclosure in primary text is preferred; alternatively, provide clear and conspicuous disclosure.

What is “Clear and Conspicuous”?

- There is no set formula; it depends on the information that must be provided and the nature of the advertisement.
- **P**lacement, **P**roximity, **P**rominence, **P**resentation

Litigation Example

FTC v. Telomerase Activation Sciences, Inc. (2018)

Claims

Company claimed its capsules, powders, and topical cream products:

- “Prevents and repairs DNA damage”
- “Restores aging immune systems, increases bone density”
- “Reverses the effects of aging skin and eyes”
- Were “research-based,” “clinically tested,” and “strongly grounded in scientific evidence”

FTC’s Stance

- The claims were unsubstantiated.
- You need proof grounded in “sound science.”
- Follow established FTC advertising principles.

Settlement

The company is barred from:

- Making any future claims about reversing aging, repairing DNA, increasing bone density, improving skin elasticity or vision, and a variety of other claims that are not based on human clinical testing
- Any other health-related claims that are not substantiated by competent and reliable scientific evidence

National Advertising Division (NAD) Case Example

Elysium Health, Inc., NAD Case # 6339 (2020)

- NAD challenged the following claims, which the company elected to permanently discontinue after NAD's challenge:
 - “Taking Basis [dietary supplement] will provide a noticeable effect on consumers' energy, cognitive function, sleep, and overall feeling of health.”
 - “Taking Basis is scientifically proven to counteract the natural human aging process.”
 - “Taking Basis provides noticeable physical health and anti-aging benefits without the need for diet and exercise.”

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